

## **REMARKS**

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the changes place the application in condition for allowance.

### **I. Status of the Claims and Formal Matters**

Claims 1, 2, 5-26 and 28-32 and 38 are under examination in this application upon entry of the amendments presented herein. As described herein, support for the claims can be found throughout the application. No new matter is added. It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. §112.

### **II. THE REJECTIONS UNDER 35 U.S.C. § 112 ARE OVERCOME**

Claims 1, 2, 5-26, 28-32 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Support for the recitation “micromachined polymer scaffold” in claims 1, 14, 25, 28 and 32 can be found throughout the specification, for example, in paragraphs 75-77, and Examples 3 and 4, which describe the microfabrication process for polymer scaffolds of the invention. In short, micromachining is used to create a mold. Once a polymer is cast on the micromached mold, a micromachined polymer scaffold results.

### **III. THE REJECTIONS UNDER 35 U.S.C. § 103 ARE OVERCOME**

#### **A. Rejection of Claims 15-17 and 32-34.**

Claims 1, 2, 5-26, 28-32 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss et al. in view of Vacanti et al. and Mastrangelo et al., and if necessary, Cima et al, Marra et al. Applicants respectfully traverse the rejection.

The present invention provides a three dimensional system comprised of interconnected layers for cell growth. One or more layers of the invention will have patterned microchannels that enable physiological systems (e.g., vascular networks) to form. Thus, three dimensional systems of the invention provide the high resolution patterning that is required to mimic complex tissues and vital organs.

It is respectfully asserted that the cited references, taken either alone or in combination, fail to teach or suggest tissue engineered systems comprising micromachined polymer scaffolds.

Weiss et al. discloses non-microfabricated, low precision devices produced by standard polymer fabrication techniques, which are joined together by micromolded polymer attachment methods. Microfabrication is only indirectly referred to as a method to produce "barbs" or interconnects which join layers. Weiss does not propose the use of microfabrication to form patterned microchannels. In short, Weiss only describes using macroscale features in tissue layers and stacking them. There is no teaching or suggestion for a micromachined polymer scaffold in Weiss et al.

Mastrangelo et al. merely provides polymer layers stacked on top of a rigid substrate. The silicon wafer of Mastrangelo et al. forms part of the structure. There is no ability to scale the process into a standalone 3D scaffold. The polymers are etched, not molded, and therefore do not provide channels having the functionality of microfabricated channels. There is no teaching or suggestion in Mastrangelo et al. for micromachining, much less a micromachined polymer scaffold.

Vacanti et al. teaches methods of solid free-form fabrication, but not micromachining. As a result, the resolution is a limited range, which is comparatively much less effective for the construction of engineered tissues than the claimed invention. Vacanti et al. therefore fails to teach or suggest structures with high resolution (less than 250 microns) formed in polymer scaffolds by micromachining.

For the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988). There must also be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowicz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993).

The cited references, taken either alone or in combination, are silent with respect to micromachining of polymer scaffolds. A major innovation was required to move from the macro-world of the cited references to the micro-world of the subject invention. Otherwise simple fabric with mesh could be claimed as presaging the claimed microchannels simply

because simple fabric has structures therewithin and can be stacked. In short, there is no motivation for the skilled artisan to look to the teachings of Weiss et al., Mastrangelo et al. and/or Vacanti et al., either with or without Cima et al. or Marra et al., to construct micromachined polymer scaffolds, much less modify the teachings of the same to achieve the micromachined systems of the claimed invention.

Nowhere in the cited references is the need to produce high resolution channel patterns for improved physiology acknowledged. The cited references do not teach or suggest this modification of their systems and consequently, there is no incentive or motivation provided for the modification. Likewise, no reasonable expectation of success in achieving such a modification can be found in the cited references. Thus, the cited combination is not proper.

Moreover, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). Here, the cited references fail to teach or suggest all limitations of the claimed invention.

In particular, the combination of the cited references fails to teach or suggest a micromachined polymer scaffold. As such, the cited references fail to teach or suggest engineered systems that are capable of producing high resolution vascular networks. *See* paragraph 196 of the specification, demonstrating a resolution of 2  $\mu\text{m}$  in micromachined polymer scaffolds of the invention. The examiner posits that Weiss teaches 3D scaffolds without microchannels, and that Mastrangelo et al. taught microchannels, and Vacanti taught pores, so putting them together results in the claimed invention. This is incorrect because the prior art involving pores or 3D macroscaffolds is completely distinct from the microchannels and other precise architecture of the subject invention.

Importantly, Mastrangelo et al. is being misapplied because it does not provide the teachings attributed to it by the Examiner. In particular, Mastrangelo et al. do not teach how to make microchannels or microstructures in a way that could form living tissue. Mastrangelo et al., however, teach instead how to make the analog of an integrated circuit chip with fluidic channels instead of transistors. Mastrangelo et al.'s approach and process are completely incompatible with cells, tissues and 3D integration because the structures are built up using microelectronics-type processes incompatible with cells, and because the mechanical and fluidic integrity of his system are destroyed once the networks are separated from the rigid substrate.

Turning to the shortcomings of Vacanti et al., the pores of Vacanti et al. are not analogous to the claimed channels. The pores are relatively random structures that, in the aggregate, do not replicate the complex and intricate structures of an organ such as capillary beds, sinusoids, renal proximal tubules and the like. Pores as scaffold structures are not the present invention. Rather, micromachining to define the scaffold precisely and produce the structures precisely is presently claimed.

In view of the above, the engineered systems of the cited references lack the functional vascular networks and improved tissue structures of the present invention and the rejections are improper.

If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). Claims 1, 25, 28 and 32 are directed to a multi-layered structure having at least one layer comprised of a micromachined polymer scaffold. Claims 2 and 5-24 and 38 depend or ultimately depend from claim 1, claim 26 depends from claim 25, and claims 29-31 depend from claim 28. As the cited references fail to teach or suggest the invention of claims 1, 25, 28, 32 and 38, claims 2, 5-24, 26 and 29-31 are by extension also non-obvious.

Reconsideration and withdrawal of the rejections of claims 1-26, 28-32 and 38 under 35 U.S.C. § 103 is respectfully requested.

#### **Request for Interview**

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

**CONCLUSION**

In view of the amendments and remarks herewith, the application is in condition for allowance. Favorable reconsideration of the application, reconsideration, and withdrawal of the objections to and rejections of the application, and prompt issuance of a Notice of Allowance are respectfully requested.

Respectfully submitted,

Date: January 4, 2006

A handwritten signature in cursive script that reads "George Chaclas". The signature is written in dark ink and is positioned above a horizontal line.

George Chaclas, Reg. No. 46,608

Amy Leahy, Reg. No. 47,739

Attorneys of Record

EDWARDS ANGELL PALMER & DODGE LLP

Intellectual Property Practice Group

P.O. Box 55874

Boston, MA 02205

Telephone: (401) 276-6653